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Sanitized Copy Approved for Release 2011/04/11 :
CIA-RDP81-00280R000200140002-9

ANTIBIOTICS IN RADIATION SICKNESS

Antibiotiki [Antibiotics],
No 6 (50), 1955, Moscow,
Pages 39-50

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(This report is based on data from foreign periodicals)

Advances in nuclear physics and use of atomic energy for peaceful purposes provide humanity with boundless possibilities. Radioactive isotopes and radiations are currently utilized on a steadily increasing scale in science and engineering. Single massive radiations which may arise under wartime or accidental conditions as well as repeated and sometimes chronic exposures to small dosages of radiations can sometimes induce cases of radiation sickness.

These circumstances urgently dictate the necessity of thorough studies of the clinics of radiation sickness and as we will see hereinafter the determination of the role of antibiotics in the course and outcome of the disorder.

In the etiopathogenesis of radiation sickness it is necessary to take into account a number of factors which determine the clinical picture. First, the dosage and nature of radioactive radiation; second, the biological reaction of the macroorganism to the radiation; third, the occurrence of endogenic autoinfection or exogenic infestation and infection course under conditions of drastically altered immunity reactions.

In view of the fact that certain salts of heavy metals, either radioactive or not, are often pharmacologically active as such and can induce a number of toxic symptoms we will omit in the description given hereinafter, the symptoms of the toxic action of these substances and consider only those injuries which are caused by ionizing action of radiations. As a result of the action of such radiations most serious metabolic disorders take place in the organism due to destruction of the initially affected cells, intoxication of the organism by products of their disintegration and the pathological reactions of individual tissue systems and the entire organism as a whole.

The review paper by Ord and Stocken (1) contains reports of profound biochemical shifts in the metabolism under the influence of X-rays. These authors subdivide the disorders induced in man as a result of a direct irradiation in 3 periods: the first period is the initial stage of the disorder the duration of which is of about 48 hours; the second is the latent period when the person feels well during 6-7 days, and finally the third is the acute period. The first period is of early symptomatics, the result of autointoxication by pharmacologically active substances, emitted from the cells primarily damaged by irradiation. The patient exhibits general malaise, with higher dosages a dazed condition. Functional disturbances characteristic of this period subside as the pathological disintegration products are being eliminated from the organism. By a number of experiments it has been ascertained that considerable disruptions occur in the metabolism of nucleic acids, glycogen etc. However these disruptions subside rapidly and during the second period the condition of the patients and also that of the experimental animals is satisfactory, although the biochemical shifts do not fully revert to normal and some disruptions of the metabolism persist. During the third, the acute period of the sickness there are noted still more

STAT

serious metabolic disturbances. Nitrogen balance becomes negative, enzymatic activity is upset, consumption of oxygen is increased, a dissociation is noted of oxidation and phosphorylation processes, inactivation of anabolic processes, disruption of the permeability of cellular membranes; occurrence takes place of edemata, ulcerations, sharp disturbances in hematopoiesis, digestion, disruptions of regeneration and growth of tissues.

Smith (2) classifies symptomatics of radiation sickness in man according to the following syndromes: (1) Damage of skin (and mucosal) integuments; (2) general effect of irradiation and its action on blood and hematopoietic organs; (3) malignant effects; (4) damage to the eyes (cataracts); (5) disruption of genital functions; (6) lowered work capacity; (7) genetic sequelae of irradiation.

A number of investigators (3,4) have described the clinical picture of the sickness following exposure to median lethal dosages of ionizing radiation or total irradiation with X-rays and γ-rays and also on exposure to lethal dosages and safe dosages.

On analyzing the experimental data of individual investigators and the consequences of atomic explosions at Hiroshima and Nagasaki these authors (3,4) consider that the average dosage that induces radiation sickness is 400-500 r. In their opinion a dosage of 1000 r (some consider it to be 800r) is absolutely lethal. On chronic irradiation a safe dosage is of 0.5r over a week. On exposure of man to 500 r blood and hematopoietic organs are first affected. Leukopenia occurs already on the second day, beginning with the second week hemorrhagic symptoms are noted, aplastic anemia develops during the 2-3rd month. In fatal cases there is observed penetration of erythrocytes into lymphatic ganglia and sinuses, erythrophagocytosis, trombopenia, increased permeability of the vessels, edemata.

In the intestines damage is noted to the crypt, ulceration of the intestines, hemorrhages (2 weeks after irradiation); the patients are nauseated and vomit. These symptoms are regarded by some investigators as a direct reaction of the intestines to the irradiation while others interpret them as a reaction of the patient to autoinfection with intestinal and other flora. There are frequently observed transitory changes in the sex glands, depilation, trophic changes and ulceration of the skin and mucosa, sometimes cataracts of the lens. All these symptoms occur in conjunction with malaise, general weakness, loss of weight and apathy. The nervous system, in particular the central nervous system is resistant to radiation but at high dosages which cause damage to the brain with disruption of circulation death may occur rapidly. (The recent investigations of Soviet scientists have ascertained a considerable sensitivity of the central nervous system and the interoreceptor apparatus to the action of ionizing radiations-Author's note).

Brown (5) having observed 50 patients subjected to roentgenotherapy and taking in account the consequences of the atomic explosion in Japan, divides the radiation sickness in 4 periods: (1) period of the initial reaction setting in following a brief latent period; (2) period of acute reaction; (3) period of subacute reaction; (4) period of chronic reaction. Symptomatics of the disorder are similar to the above described.

As had been pointed out the course of radiation sickness is very often complicated by infectious diseases which render the prognosis

STAT

less favorable and not infrequently constitute the cause of death. In seeking means for preventing and treating infectious diseases in persons afflicted by radiations a number of investigators have studied the influence of radiations on the microflora and the defensive mechanisms of experimental animals (6-12). It has been found that irradiation of the animal induces a sharp lowering of its defensive capabilities. In connection therewith the microflora present within the organism and introduced thereinto from outside, including also the pathogenic, begins to undergo intensive proliferation as a result of which toxemia and infection disorder set in. Gravity of the disorder and changes in the microflora are as a rule in a direct correlation with the irradiation dosage. To determine the influence and role of antibiotics in the treatment of these infections mice, chicks, rabbits, dogs and other animals, were used.

Bennison and Coatney (6) inoculated chicks with Pl. gallinaceus and Pl. lophurae. On the day of the inoculation or on the next day a portion of the birds were irradiated with a dosage of 400 r, and thereafter at definite intervals of time, determinations were made of the amount of parasites present in the blood. In the irradiated chicks the number of parasites in the blood was considerably higher than in the controls. The same relationship was retained on treatment of both groups of chicks with quinine.

Gonshery and Marston (7) investigated the blood of mice following their irradiation with different dosages of X-rays. The data of these investigations are shown in table 1.

TABLE 1

Cultures of Microbes Found in the Blood of Mice Following their Irradiation with X-rays

X-ray dosage r	Percent of mice that died	Bacillus pyocyaneus	Bacillus coli	Alpha-streptococcus	Bacillus paracoli	Proteus	Staphylococcus	Other Microbes
1400	100	4	51	4	14	14	4	9
1100	100	27	54	0	8	4	4	3
800	100	31	31	16	18	2	0	2
700	100	24	24	33	7	2	2	8
615	88	31	22	21	12	2	5	7
550	48	29	27	25	5	2	7	5

The principal causative agents of lethal infectious were the colon bacillus, proteus and α- streptococcus. Almost in all the mice which died during 6-9 days microbes were found in the blood, whereas during the first three days of sickness microbes were rarely found in the blood. Thus in the irradiated animals septicemia progressed at a rapid rate. This is well illustrated by the experiments of Congdon and Williams (12), who irradiated 2 groups of mice with a dosage of 900 r. 5 mice were killed and dissected every day. Study of the internal organs showed that on the third day after irradiation pathogenic microbes were found only in the small intestines, on the fourth day in the brain, small intestines, spleen, liver, lungs and bone marrow, and on the fifth day in all the organs. On decrease of the dosage to 550 r bacteriemia usually occurred on the seventh day. Gordon and Miller (13) have studied the influence of somatropic hormones on the survival of mice. Of the 45 mice irradiated with 550 r (distance 15 cm, rate 30 r/min) 38 died. From the dead mice were isolated 39 cultures: 11 cultures

STAT

of proteus, 15 - colon bacillus, 1 - aerobact. aerogenes, 3-enterococci, 8 - Paracoli, and I - β - hemolytic streptococcus.

Thus in the irradiated animals there often arises endogenic and exogenic infection which leads rapidly to death as a result of a sharp lowering of the resistance of the macroorganism.

It is quite natural that control of the infection complications is one of the most important parts of the composite treatment of radiation sickness. In addition to a number of medical remedies use is made of chemicotherapeutic preparations and antibiotics. In so doing it is necessary to adhere to a fundamental principle, namely to check the sensitivity of the microbe to the antibiotic utilized. It is possible that due to depression of the defensive capabilities of the organism it will be necessary to increase the dose of antibiotic or to use a combination of synergistically acting antibiotics and chemical preparations. It is necessary not only to take into account the antibacterial range of the antibiotic but also the individual sensitivity of the causative agent to this antibiotic. The widest use in the treatment of infections of the irradiated have found the following antibiotics: penicillin, streptomycin, and also antibiotics of a wide range of action (aureomycin, terramycin, chloramphenicol). These antibiotics taken singly and in combination at most diversified doses have been tested in the treatment and prophylaxis of infections. These tests were conducted on different models, at different time intervals and following different dosages of irradiation. It has been found that the efficacy of different antibiotics is not the same. Below are described the results of the tests of different antibiotics.

Penicillin

The use of penicillin in the treatment of radiation sickness complicated by infection was found to be effective (14). Mice were irradiated with 450 r and infected thereafter with 100 LD_{50} of β-hemolytic streptococcus. Administration 24 hours after inoculation of 60-200 units of benzyl penicillin lowered the death rate of the animals: in the group of the treated animals the mortality was 65% and in the untreated group it was 100%. Table 2 shows the results of the treatment of complications of radiation sickness with penicillin.

TABLE 2
Penicillin Treatment of Complications of Radiation Sickness

Experimental animals	X-ray irradiation dosage r	Penicillin Treatment	Survived as a result of treatment, %	Literature Reference
Mice	450	Beginning 24 hours after inoculation 60-200 units administered daily for 3 days	L - 36 K - 0	(14)
Rats	550	3000 units benzylpenicillin + 1000 units of penicillin K daily, during 21 days	L - 53 K - 20	(15)
Rats	550-625	15-30 mg/100 g for 20 days	L - 67 K - 10	(16)

Conventional symbols: L - treated, K - controls.

STAT

Maisin, Mandart et al., (15) irradiated rats with 500-600 r and treated them thereafter during 21 days by a daily administration of 3000 units of benzyl penicillin and 1000 units of penicillin K. Administration of penicillin reduced the mortality in rats from 80 to 47%, but the results were not as good as in the treatment with streptomycin, when only 35% of the animals died.

Smith et al., (16) irradiated rats with different dosages of X-rays (550-625 r); a portion of the animals was treated with penicillin for 20 days (15-30 mg/100 g daily). While 100% of the control animals died, 67% of the treated survived. Penicillin treatment reduced the frequency of diarrhea occurrence in rats (63% in the treated with penicillin as compared with 71% among the control rats). Thus penicillin is an effective remedy for the treatment of the complications of radiation sickness, but as will be shown hereinafter, it is inferior in therapeutic action to streptomycin and some other antibiotics.

Streptomycin

Numerous data are available which show that streptomycin is highly active against the complications of radiation sickness, especially in the treatment of diarrhea. Summative data shown in table 3, provide a confirmation thereof. Efficacy of streptomycin in the treatment of radiation sickness is revealed even more clearly in the work of Gonshery and Marston (17).

TABLE 3

Streptomycin Treatment of Complications of Radiation Sickness

Experimental Animals	X-ray irradiation dosage r.	Streptomycin Treatment	Result of treatment	Literature reference
Mice	475	Beginning 6 hours after irradiation 1.25-5.0 mg daily for 3-8 days	Good	(17)
Mice		Subcutaneously, 250-300 mg/kg daily	Survival increased by 43-65%	(18)
Rats	600	6 mg daily for 21 days	Survival 65% (in controls 20%)	(15)
Mice	450	7000 daily for 24 days	Survival 70% (in controls 23%)	(8)
Mice	450	6000 daily for 34 days	Survival 84% (in controls 19%)	(8)
Mice	600	4-7 mg daily for 10-25 days	Survival 20-50% (in controls 50%)	(16)

Rats	550-625	7 mg daily for 10-25 days	Survival 45% (in controls 0)	(16)
Mice	550-625	5 mg daily for 25 days	Survival 33% (in controls 20%)	(7)
Mice	475	1.25 mg 5 minutes after infection	Survival 47% (in controls 8%)	(19)
Mice	550	6 mg daily for 20 days	Survival 52% (in controls 15%)	(137)

They treated a portion of the irradiated mice (550-625r) with streptomycin (5 mg daily from the 3rd to the 20th day following irradiation) and studied thereafter the microflora. The results of the treatment are shown in table 4.

TABLE 4

Streptomycin Treatment of X-ray Irradiated Mice

Animal group	Number of Irradiated animals	Died	Negative	Positive	Bacillus Pyocyaneus	Bacillus Coli	Protens	Streptococcus	Staphylococcus	Other
Control	446	363	156	207	35	48	35	44	19	26
Treated	446	300	213	87	31	11	6	9	7	23

Miller and Hammond (8) subjected to X-ray irradiation (450r, 20 Kv, 15 mA, distance 67 cm) mice in which the DL_{50} had previously been determined as being 400 r. From the fourth to the twenty-eighth day following irradiation they administered to the mice, subcutaneously, 6-7 mg of streptomycin daily. After 30 days 77-81% of the controls died, while among the treated mice given 6 mg daily 16% died, and of those given 7 mg daily, 30% died.

Marston and Gonshery (17) irradiated mice with 250 and 475 r and thereafter a portion of the animals was inoculated with staphylococcus aureus, proteus, paracoli and coli bacilla, α-streptococcus and bacillus pyocyaneus. Six hours after inoculation administration of streptomycin to the animals was started (from 1.25 to 5 mg daily for 3-8 days). Inoculation of the mice after irradiation caused a sharp increase of their mortality, streptomycin therapy was found to be effective in the treatment of infection induced by staphylococcus aurens, paracoli and coli bacilla and protens, but was not effective in cases inoculated with bacillus pyocyaneus. Use of streptomycin at a dosage of 1.25 mg daily for 3 days was found to be just as effective as an administration twice daily of 2.5 or 5 mg. Efficacy of streptomycin at low irradiation dosages (250r) was greater than at higher (475r).

Smith et al. (16) on comparing the action of streptomycin, penicillin and aureomycin, used singly and in combination have found that the best results are obtained with streptomycin. On administration of streptomycin during 6 days, 7 mg daily, 45% of the animals survived (diarrhea was observed in 31% of the animals); in the control group 100% of the animals died, and of these 67% had diarrhea.

Marston and Ruth (19) after irradiating mice with 475 r (distance 50 cm) inoculated them with proteus and after 5 days started the streptomycin treatment, with 1.25 mg daily. Of the 19 inoculated not irradiated mice 2 died (10%) while of the inoculated and irradiated 90-100% died. Streptomycin therapy applied to mice inoculated 7-10 days after irradiation was more effective than in those inoculated after 5 days. To enhance the resistance of the organism some mice were given prior to inoculation an injection of a homogenate of the spleen of irradiated animals into the caudal vein. This resulted in an increase of the effectiveness of streptomycin treatment and the survival rate was increased to 47% (8% in the controls). All this also indicates that streptomycin therapy depends upon the defensive capabilities of the organism.

Gordon and Miller (13) investigated the influence of somatotropic hormone and streptomycin on mice subjected to irradiation. Mice weighing 20-25 g were divided in groups of 20 mice each and irradiated at a distance of 51 cm with 30r min (total dosage 550 r). Eighty-five mice were given the somatotropic hormone (0.6 γ daily) and streptomycin (6 mg daily), 45 mice were given only the hormone, 106 only streptomycin, and 45 mice served as controls. Duration of the treatment was of 20 days. Results of the treatment are shown in Table 5.

TABLE 5

Results of the Treatment of Complications of Radiation Sickness with Somatotropic Hormone and Streptomycin

Index	Somatotropic Hormone and Streptomycin	Streptomycin	Somatotropic Hormone	Control
Number of mice	81	106	45	45
Died	64	52	43	38
Cultures tested	43	27	43	38
Positive cultures	12	5	34	38
Isolated microbes (number of cultures):				
Protens	-	-	15	10
B. coli	1	-	3	5
Alc. faecalis	6	-	2	-
A. aerogenes	-	-	-	1
Salmonellae	3	2	4	10
Enterococcus	2	3	-	3
B. Paracoli	-	-	10	8
-Hemolytic streptococcus	-	-	-	1

The somatotropic hormone was found to be ineffective. Its use with streptomycin did not reduce the mortality but prevented loss of weight.

Thus in the treatment of the complications of radiation sickness streptomycin was found to be an effective antibiotic superior to that of penicillin. While increasing the survival rate of irradiated animals, including those which were infected by inoculation. Streptomycin contributes to the prevention of one of the most refractory symptoms of radiation sickness, namely of diarrhea, and in combination with the somatotropic

STAT

hormone it prevents loss of weight. In individual instances the effect was variable and slight.

Antibiotics of Wide Antibacterial Range

In view of the diversity of the bacterial flora, consisting of gram-positive and gram-negative bacteria, usually found in irradiated animals, the use of wide range antibiotics (aureomycin, chloramphenicol and terramycin) has attracted the attention of a number of investigators. The results of these researches are shown in table 6.

Miller and Hammond (8) on comparing the action of chloramphenicol, streptomycin and aureomycin, have found that chloramphenicol is a very effective agent. On treatment with chloramphenicol, after 30 days only 36% of mice died (30% on using streptomycin therapy) after being irradiated with 450 r, while the rate in the controls was of 60%. Treatment with aureomycin yielded variable results and its efficacy was clearly inadequate.

TABLE 6

Treatment of Complications of Radiation Sickness with Wide Range Antibiotics

Experimental Animals	X-ray dosage r	Treatment	Results	Literature Reference
Rats	660 (60 r/min)	T per os 5 doses of 100 mg 48 hrs before irradiation	Mortality 48% K(72%)	(20)
Mice	450	A at 50-250 γ daily for 3 days	Little effect	(14)
Rats	660	T 0.2-200 γ, 72-4 hrs before irradiation	Mortality 45-80%	(11)
Rats	660	X, 100 mg kg daily	Mortality reduced by 24-25%	(18)
Rats	660	T subcutaneously 25 mg/kg daily	Same by 25%	(18)
Rats	660	A subcutaneously 50 mg kg daily	Same by 30%	(21)
Dogs	450	A per os 2 mg/kg for 28 days	Same from 58 to 44%	(22)
Mice	450	X, 2 mg daily for 24 days	Same from 60 to 36%	(8)
Rats	550-625	X, 5 mg daily for 7 days	Same from 100 to 52-86%	(16)
Rats	550-625	T, 20 mg daily for 10 days	Same from 100 to 17%	(16)
Rats	550-625	A 30 mg daily for 11 days	Same from 100 to 21%	(16)
Dogs	550-625	T 100 mg/kg daily for 28 days	Same from 92 to 50%	(23)

Conventional symbols: T-terramycin; X-chloramphenicol; A-aureomycin; K-untreated controls

Gustavson and Koletsky (11) beginning 72 hours prior to and terminating 4 hours before irradiation with 660 r treated rats with 0.2, 2.0, 20 and 200 γ terramycin. The results of the prophylaxis are apparent from Table 7.

STAT

Effect of Different Doses of Terramycin on the Mortality of Rats Irradiated with 660 r

Dose of Antibiotic,	Number of Rats Surviving after 30 days	Percent of Rats that died	Average survival in days
	First Experiment		
Control	5	75	8.7
0.2	4	80	9.8
2	8	60	11.2
20	7	65	11.7
200	11	45	13.3
	Second Experiment		
Control	5	80	12.8
20	7	72	10.0
200	18	28	14.4

Thus only the large doses of terramycin (about 200γ) were found to be effective.

All 3 antibiotics were effective in the experiments of Miller and Hammond (18, 21) the mortality of the animals being reduced to 24-30%.

Gustavson and Koletsky (20) wishing to check the prophylactic action of terramycin divided 200 white rats weighing about 200 g in 2 groups (of 100 animals each). Terramycin treatment was started 48 hours prior to and terminated 1-4 hours before irradiation. After irradiation no antibiotic was given. The investigation lasted for 30 days. The total irradiation dosage was of 660 r (60 r/min) at a distance of 44.3 cm. Mortality of the controls was of 72%, of the treated animals 18%. Average survival time of the control animals was of 10.6 days that of the treated, 15 days. Between the fourth and the twelfth day, 6.2% of the control rats died, and 2.6% of the treated. Diarrhea was more severe among the treated rats than among the controls, which is possibly due to a reaction to large doses of terramycin. From the fifth day the treated rats gained more weight than the controls. By the sixth to eighth day the weight of the treated animals was on the average 15 g above that of the controls. After 12 days following irradiation the weight of the animals in both groups reached the same level.

Furth and Coulter (22) have investigated the therapeutic action of aureomycin in dogs. Twelve irradiated dogs (total dosage 450 r; 7.15 r/min) were treated over 28 days, with 25 mg/kg of the antibiotic every 6 hours; 12 other dogs served as controls. In the control group 58% of the dogs died, and 44% in the group of treated animals. The first control dog died 7 days earlier than the first treated. Positive bacteriological findings in the blood of the control animals amounted to 14.8% while in the treated they amounted to 6.3%. Essentially staphylococci and bacteria coli were found in the culture tests. All the dogs that died showed on autopsy symptoms of hemorrhagical diathesis with extravasations in the lungs, spleen, kidneys, lymphatic ganglia and gastrointestinal tract, but in the control animals these symptoms were more pronounced. The authors (23) used terramycin on 27 dogs of which 13 served as controls. The dogs were irradiated with 480 r and immediately thereafter given every 6 hours for 28 days, 250 mg of terramycin each, per os, in capsules (100 mg kg daily). Between the tenth and the twentieth day dogs of both groups showed somnolence and anorexia, no differences were found in blood pathology. The first of the control dogs died on the eleventh day, and the first of the treated on the fifteenth

STAT

day. After 30 days 92% of the control animals had died and 50% of the treated. Study of the resistance to terramycin of the cultures isolated from the dead dogs showed that in the control animals 30% of the cultures were resistant to 25 γ/ml of terramycin while in the treated 69% of the cultures were resistant.

Thus the antibiotic of a wide range of activity were found to be less effective than streptomycin and penicillin. Terramycin was effective only in large doses (about 200 γ). Of the wide range antibiotics chloramphenicol was more effective than the other.

The etiological diversity of infectious complications in radiation sickness naturally led the investigators to an attempt of utilizing a combined application of antibiotics for the treatment of these complications. The results of some experiments carried out by individual researchers are shown in table 8.

Of the various combinations of antibiotics penicillin with streptomycin, polymyxin with neomycin and terramycin with penicillin were most frequently utilized. However a combined use of antibiotics, as a rule, was no more effective than the administration of the better one of the combination. Streptomycin was found to be the most effective.

Table 8

Treatment of Infectious Complications of Radiation Sickness with Combined Antibiotics

Experimental Animals	X-ray dosage r.	Treatment	Results	Literature reference
Mice		P + S 40000 units/kg daily	Survival increased by 30-40%	(18)
Mice	450	P 10000 units + S 5000 γ for 24 days	Survival increased from 34(K) to 75%	(8)
Rats	550-625	S 20 mg 100 g + P 20 mg/100 g for 14 days	Same from 0 (K) to 29%	(16)
Rats	550-625	Pol. 0.4 mg + N 1.25 mg for 21 days	Same from 0 to 24%	(16)
Rats	550-625	T 20 mg/100 g + P 20 mg/100 g for 10 days	Same from 0 to 20%	(16)
Mice	550	S + ST	Same from 15 to 21%	(13)

Conventional symbols: P-penicillin; S-streptomycin; Pol-polymyxin; T-terramycin; N-neomycin; ST-somatotropic hormone.

In studying the action of antibiotics in radiation sickness the latter is usually induced by X-rays; it is necessary to determine the action of antibiotics when the disorder is induced by radioactive radiation. Very few researches have been published on this question. As a rule the picture of radiation sickness and the effects of antibiotics on its complications did not differ substantially from the course of the disease induced by X-rays at sublethal dosages.

Koletsky and Christi (24) administered intraperitoneally to 248 rats (weighing 125 g) radioactive phosphorus (P^{32}). The animals were divided in two groups: control and experimental. The animals of the latter group were treated twice a day with 12 mg of streptomycin and once a day with 20000 units of penicillin. Of the 124 treated rats 49 were given during 3-10 days antibiotics as a prophylaxis, while to the remaining 75 rats administration of antibiotics was started immediately after the introduction of

P^{32} and the treatment was continued for 3 weeks. As is apparent from table 9, mortality of the treated rats are lower than that of the controls. Of the 124 controls [illegible] ([illegible]%) died, while of the same number of treated animals (36%) died. The difference between mean duration of survival of the controls (15 days) and of treated animals (19 days) was not large, but the control animals started to die sooner. In the treated rats a lesser decrease in weight was observed as well as fewer instances of diarrhea; they showed better appetite and had fewer cases of hemorrhages than the controls. It is assumed that death of the animals is caused by toxemia.

It should be noted that efficacy of the treatment is directly dependent on the dose of radioisotope and to a lesser extent on whether the treatment is started prior to or immediately after the administration of the radioactive substance.

On analyzing the published communications concerning the use of antibiotics in the clinic of radiation sickness it must be admitted that notwithstanding the drastic changes in the reactivity of the macroorganism and the inhibition of some immunobiological mechanisms and also in spite of the occurrence of a number of mutations of microbes, the antibiotics are indispensable and necessary components of a composite treatment of radiation sickness.

TABLE 9

Penicillin and Streptomycin Treatment of Rats Injured by Radioactive Phosphorus (P^{32})

Experiment #	Number of Rats	P^{32} Dose MC/g	Treatment	Percent of Rats that died after 10 Days	15 Days	21 Days	30 Days
1	30	3.0	Treatment	0	0	0	0
			Control	0	20	27	27
2	30	3.8	Treatment	0	0	7	13
			Control	7	20	33	47
3	29	3.5	5 Days Prior	0	0	14	14
			Control	0	36	43	67
4	30	5.5	Treatment	0	27	47	47
			Control	0	53	67	67
5	30	5.0	Treatment	0	13	27	33
			Control	0	40	47	73
6	16	4.5	14 Days prior	0	0	50	50
			Control	0	38	38	75
7	30	6.0	Treatment	0	53	53	60
			Control	7	53	80	80
8	23	4.5	3 days prior	0	14	14	33
			Control	7	60	100	–

Because of the action not only on the microorganism but also on the macroorganism over the nervous system, use of antibiotics in radiation sickness requires careful observations and checking of the dosage, sensitivity of the microbe to the given antibiotic, and the account of toxic and allergic reactions during the treatment.

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